MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

TO : All Screeners

DATE: June 24, 1976

FROM : Head, Screening Section
DEB, DR&DP, DCT, NCI

SUBJECT: Biological Data Processing System Calculation Changes

Effective immediately, several changes, related to Late Treatment Control Pack processing but applicable to all control packs, have been incorporated into the mean and median survival time calculations performed by the Biological Data Processing System. This instruction outlines those changes.

1. Body weight change differences (used in establishing chronic toxicity) will only be calculated and displayed when the control group and the treated group are both weighed on the same days, or within one day of one another, otherwise an indication of not applicable (N.A.) will be substituted. This determination will be made as follows:

   Control group weights will be assumed to have been taken four days prior to the toxicity day specified in the input and on toxicity day itself. Treated group weights will be assumed to have been taken on first treatment day and again four days later. When comparison indicates that the second weight day for each group is equal or within one day of one another, weight change differences will be calculated and displayed. When the two sets of days are not the same, no body weight change difference calculation will be attempted and an N.A. will be displayed in the animal weight difference (T-C) field on the SDS and the SEA.

2. The mean survival time calculation (see Attachment A for formula) has been modified for both the control and treated groups of animals. Whereas A in the mean survival time calculation (Section 11.100, Cancer Chemotherapy Reports, Part 3, Vol. 3, No. 2, September, 1972) has traditionally been toxicity day plus one and varied as toxicity day varied, it is now being established according to a fixed table (see Attachment B) for control groups. Day A will be the early death day listed in the table plus one, i.e, for Test System 3B131 Day A will be 11, or will be established as Day 1 if no entry can be found in the table. Control deaths occurring on or before the day identified in the table column "Early Death Day" are considered early deaths and excluded from the mean survival time calculation.

Control deaths occurring after that day are always used in the mean survival time calculation without regard to the day of first treatment associated with any of the treated groups.

The calculation for the treated group has been modified in that "A" is established from the first treatment day as follows:

If day of first injection is less than three, the value of Day A is day of first injection plus five.

otherwise

The value of Day A is the same as the day of first injection plus one.

3. That aspect of acute toxicity (as defined in Section 4.301, b, 1) associated with 34% deaths on or before toxicity evaluation day will be bypassed whenever the day of first treatment is Day 3 or greater. This is necessary as very often a later treatment day could result in attempting to measure acute toxicity in the range of normal tumor deaths.

4. A final change involving the late treatment packs is that treated group deaths that occur prior to first treatment day will be excluded from influencing the survival calculation. The original number of animals is reduced and the death pattern adjusted for purposes of performing the calculation. This is best illustrated by an example:

Original Animal Count	Survival Pattern					Day First Treatment
	Day	0	5	9	11	15
10	# Surv.	10	8	5	3	0	7

All deaths occurring prior to Day 7 will be eliminated (for purposes of the calculation only) yielding:

Adjusted Original Animal Count	Adjusted Survival Pattern				
	Day	0	9	11	15
8	# Surv.	8	5	3	0

Without the adjustment the median survival time of the treated group is 10.8 days.

With the adjustment the median survival time of the treated group is 11.3 days.

Attachment A

MEAN SURVIVAL TIME FORMULA

$$\text{Mean survival time (days)} = \frac{\Sigma S + A S_{(A-1)} - (B+1)\,NT}{S_{(A-1)} - NT}$$

Definitions:

Day A = Day on which deaths are no longer considered due to drug toxicity.

Day B = Day beyond which control group survivors are considered "no-takes."

ΣS = If there are "no-takes" in the treated group (as defined in Protocol 11.103), ΣS is the sum from Day A through Day B. If there are no "no-takes" in the treated group, ΣS is the sum of daily survivors from Day A onward.

$S_{(A-1)}$ = Number of survivors at the end of Day (A - 1).

NT = Number of "no-takes" according to the criteria given in Protocols 7.300 and 11.103.

SURVIVAL SYSTEMS

EARLY DEATH DAY TABLE

Host Group	Tumor Code	Site	Tissue	Level	Acceptable Survival Range (Days)	Early Death Day
3	AK	1	3	G	17-21	10
3	B1	1	2	G	14-24.5	10
3	B1	2	2	G	21-31	13
3	B1	7	2	G		
3	EM	7	6		14-25	10
3	LE	1	1	5	8-11	05
3	LE	7	1	4	7-10	04
3	LE	9	1	7	3-7	03
3	LE	2	1	5	8-11	05
3	LL	2	2		19-35.6	14
3	LL	2	6		19-35.6	14
3	LL	6	2		18-28	12
3	LL	9			19.5-23.5	13
3	LX	1	1	6	8-11	05
3	PS	1	1	6	9-13	07
3	PS	7	1	5	9-14	05
3	PS	9	1	6	9-14	05
5	DL	1	1		8-11	05
5	DL	2	6		12-16	07
5	WA	1	1	6	5-9	04